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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/928,367	08/14/2001	David Duffy	11641/36	6423

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/928,367	DUFFY, DAVID	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-22,27 and 33-35* is/are pending in the application.

4a) Of the above claim(s) *8-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,27 and 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/2/04 has been entered.

Status of Claims

Claims 1, 5-22, 27 and 33-35 are pending.

Claims 8-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 5.

Claims 2-4, 23-26, 28-32 have been cancelled.

Claims 1, 5-7, 27 and 33-35 are under examination.

Claim Rejections - 35 USC § 112, first paragraph

Claims 1, 5-7, 27 and 33-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed "underlying the holes of the gasket" is not supported in the as-filed specification. Likewise, a claim to gasket with holes that has an orientation of wells of a 96-well and the other recited wells. Furthermore, the recited polymer gasket placed on a substrate is at odds with the specification at page 8, paragraph 21.

Applicants point out the support at paragraph 21. However, this section does not support the presently claimed limitations. This section recites surface without using wells. Also, the section merely refers to the copending application, which recites broadly a polymer gel mask. The copending application has not been incorporated as essential material to the present application. Accordingly, the steps in claims 1 and 33-35 are not supported in the as-filed specification. Cf. Example 3 in the specification with the newly added claim 35.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-7, 27 and 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1, step (b) is unclear as to whether the target molecule is immobilized in the gasket holes attached to the substrate. It is unclear as to the essentiality of the gasket holes to the process step. Also, it is not clear as to the type of modification imparted on the target by the mere process step of contacting a target molecule with another compound.

2. Claims 5-7 are unclear as to the function of the target being detected. Claim 1 already recites the target molecule as the enzyme, Tyr kinase.

3. Claim 34 is unclear as to what constitutes a self-assembled monolayer formed on the substrate, absent definition in the specification.

4. Claim 35 is at odds with Example 3 of the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5-7, 27, and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruggieri et al or Xue et al (6,630,296) in view of either Mitsuhashi et al (WO 01/07164).

Xue et al discloses at col. 2, line 60 up to col. 4, line 30 a method that includes performing a plurality of enzyme reactions in the presence of plurality of enzymes substrates in a set of substrates, under conditions effective to convert an enzyme substrate to a corresponding product, where the product of each substrate and the substrate have different separation characteristics from each other and from the other substrates in the set and their corresponding products. After performing the reactions, the products, and preferably also the substrates in the reactions are separated in a single separation medium. For each separated product and substrate, a separation characteristic effective to identify that product and substrate and a signal related to the amount of the product and substrate is detected. From this, the amount of substrate converted to the corresponding product in each of the reactions can be determined. The enzyme may be, for example, a kinase from different functional groups of kinases, protein kinase C, ERK/MAP kinases, and protein-tyrosine kinases. The kinase may be a protein kinase enzyme in a signaling pathway, effective to

phosphorylate an oligopeptide substrate, such as ERK kinase. Other kinases of interest may include, for example, Src kinase, JNK, MAP kinase, cyclin-dependent kinases, P53 kinases and MEK.

Ruggieri et al discloses at col.3, lines 10-40 a method of in which SRK (a class of proteins involved in cell signal transduction pathways such as MAPK pathways) activates inactive MAPKK polypeptides, i.e., an MAPKK stimulatory activity. This activity can be direct, e.g., by directly acting upon the MAPKK (e.g., phosphorylating it), or it can be indirect where activation is accomplished by acting upon one or more intermediates which then stimulate MAPKK activity. An MAPKK stimulatory activity means, e.g., that SRK, and polypeptides thereof, activate or stimulate a MAPKK protein kinase activity. MAPKK stimulatory activity can be measured in vivo or in vitro as illustrated in the examples. MAPKK proteins stimulated or activated by SRK include, e.g., MEK. In one type of assay, SRK is co-expressed in a cell with an MAPKK; the MAPKK is isolated, and then assayed for kinase activity using an appropriate substrate, e.g., ERK when MEK is used. The amount of stimulatory activity can be determined by measuring the MAPKK kinase activity from cells transfected with and without SRK. MAPKK stimulatory activity can also be measured in cell-based assays. For instance, cell viability in cell lines defective in MAPKKK

activity, such as cell lines lacking Raf, are rescued when transformed with SRK. SRK is a member of a cell signal transduction pathway, one activity of which is to activate gene transcription. Expression analysis can be performed conventionally. For example, high-density oligonucleotide chip arrays can be designed to monitor expression. Such chips can contain all or subsets of the human genome.

Ruggieri at col. 14, line 10 up to col. 15, line 55, discloses a method of regulating a biological response in which SRK, or a homolog thereof, participates, e.g., by being a participant in the biochemical pathway which leads to the ultimate cellular response. For instance, an aspect of the invention relates to methods of modulating signal transduction in which SRK is involved. Since such signal transduction can lead to various biological responses, including transcriptional activation of certain genes. Thus, the invention relates to methods of controlling expression of these genes by modulating SRK activity. Any of the methods described in, e.g., U.S. Pat. Nos. 5,767,075; 5,753,446; 5,728,536; 5,667,314; and 5,459,036 can be utilized e.g., using SRK, biologically-active fragments thereof, or a homologs thereof. Signal transduction mediated by SRK can be modulated by administering various agents, including a dominant negative SRK gene (see, examples). The method relates

to detecting a protein kinase activity in a SRK polypeptide, or a biologically-active polypeptide fragment thereof. Typically, a method of detecting kinase activity in a SRK polypeptide comprises, reacting a human SRK polypeptide, or a biologically-active polypeptide fragment thereof, and a substrate under conditions effective said SRK polypeptide to phosphorylate said substrate; and detecting said phosphorylation of said substrate. Effective conditions include, e.g., appropriate substrates, ATP, co-factors, etc. For SRK kinase assays, substrates can be, e.g., MAPKKs, such as MEK. Kinase activity means, e.g., the ability of SRK to transfer a phosphate group from a phosphate donor (e.g., ATP) to a phosphate acceptor (e.g., MBP). Ruggieri et al also discloses methods of identifying substrates for SRK kinase activity. SRK can be contacted with a test substrate, either in vivo or in vitro, under conditions effective for phosphorylation to occur. After a suitable time, the substrate can be isolated and probed for the presence of a phosphate residue. As mentioned, a preferable method of detecting phosphorylation is to use radioactive ATP. See, examples for further guidance. The method further relates to identifying agents which modulate a MAPKK stimulatory activity of a human SRK polypeptide, or a biologically-active polypeptide fragment thereof, comprising, administering a test agent to a cell expressing (1) a human SRK

polypeptide, or a biologically-active polypeptide fragment thereof, and (2) an MAPKK polypeptide, under conditions effective for said SRK polypeptide to stimulate protein kinase activity of said MAPKK polypeptide; detecting said protein kinase activity; and identifying whether the test agent modulates said stimulatory activity of said SRK polypeptide by comparing the amount of kinase activity in the presence and absence of the test agent. MAPKK stimulatory means, e.g., the ability of SRK to activate the kinase activity of MAPKK, itself. Such stimulation can be direct or indirect, e.g., where SRK stimulates a factor which, in turn, stimulates MAPKK. The stimulatory effect is relatively specific for the MAP kinase cascade. The term "administering" as used, means, e.g., any suitable delivery technique which is adequate to place the agent in a location where it can elicit an effect. For example, administering can mean contacting a cell or host in an effective manner with the agent of interest, whereby the agent can modulate the activity of interest. See further cols. 25 and 26, Example 1 and 2, respectively.

Ruggieri or Xue does not teach immobilizing the kinase to a substrate with a gasket in a multiwell plate. However, Mitsuhashi et al discloses at page 2, lines 3-5; page 3, lines 21-23 and page 5, lines 28-35 a gasket adapted for use with a multiwell

microplate. The use of gasket solves the problem of cross-contaminant, which may occur between adjacent nozzles on the underside of a filter plate.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use an array with a gasket in the method of either Ruggieri or Xue. The use of array is conventional in the art and is employed for high throughput screening of compounds. Furthermore, the advantage taught by Mitsuhashi et al in using a gasket in an array or multiwell plates would provide the motivation to one having ordinary skill in the art.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A. Roberts et al discloses a differentiation enhancing factors.

B. Abo et al disclose polypeptides which resemble rho and which interact with cell signaling pathways and proteins.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0812. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
July 9, 2004